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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/840,872	04/25/2001	Antonio J. Grillo-Lopez	P 0280609/2000-30-154A	4921

909 7590 11/29/2006

PILLSBURY WINTHROP SHAW PITTMAN, LLP
P.O. BOX 10500
MCLEAN, VA 22102

EXAMINER

UNGAR, SUSAN NMN

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 11/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/840,872	GRILLO-LOPEZ, ANTONIO J.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 11 September 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 56-60 and 62-74 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 56-60, 62-74 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions filed on July 10, 2006 and September 11, 2006 are acknowledged and have been entered. An action on the RCE follows.

2. Claims 56-60 and 62-74 are pending and currently under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The following rejections are being maintained:

Claim Rejections - 35 USC 103

5. Claims 56-60, 62-74 remain rejected under 35 USC 103 for the reasons previously set forth in the paper mailed April 10, 2006, pages 2-5.

Applicant summarizes Examiner's position drawn to the rejection under 35 USC 103 in a number of office actions starting with the position held in the first official action mailed 10/23/02.

Applicant reiterates arguments drawn to the lack of nexus between intrathecal treatment of CNS lymphomas by anti-Fas antibodies and anti-CD20 antibodies. The argument has been previously considered but has not been found persuasive for the reasons of record. In particular to reiterate, given the know efficacy of antibodies, that is anti-CD20 antibodies, against B-cell lymphomas (Anderson), given the know efficacy of treatment of CNS B-cell lymphomas by intrathecal administration of antibodies, that is anti-Fas antibodies (Caliguiri), it would have been prima facie obvious to one of ordinary skill in the art at the time

the invention was made to have substituted antibodies known to be useful to treat B-cell lymphomas, that is, anti-CD20 antibodies, for the antibodies known to treat B-cell lymphomas, that is anti-Fas antibodies, with a reasonable expectation of success for the reasons of record.

Applicant argues that Examiner did not previously consider arguments drawn to inability to extrapolate the suitability of one antigen target for another due to differences in antigen expression profiles including localization, density, expression levels etc. The argument has been considered but contrary to Applicant's arguments these arguments were in fact previously considered, it is suggested that Applicant review page 4 of the previous office action wherein these arguments were considered but were not found to be persuasive.

Applicant reiterates arguments drawn to different modes of action of anti-Fas and anti-CD20 antibodies. The arguments have been previously considered and not found to be persuasive for the reasons previously set forth.

Applicant reiterates arguments drawn to the unexpected success of anti-CD20 antibodies for the treatment of CNS lymphomas and the differences in modes of action of the anti-Fas antibodies of the prior art and the anti-CD-20 antibodies instantly claimed. Applicant points to Pollack et al, submitted after final, to support the surprising nature of the claimed invention. Applicant specifically states that Pollack et al demonstrate that at the time the instant application was filed that the unpredictability of treating brain tumors was well known in the art. Applicant specifically points to the teachings that reveal differences in the immune environment of the brain compared with the extra-CNS environment. The argument has been considered but has not been found persuasive because although Pollack et al specifically provide information drawn to the

unpredictability of treating brain tumors, as previously set forth, the Garber Declaration at item 33 specifically points to Shan et al, Blood, 1998, 91:1644-1652 which states that the mechanisms of action of anti-CD20 antibodies include induction of apoptosis (p. 1844, col 2). Thus, contrary to Applicant's arguments, the mechanisms of action of the anti-Fas antibodies and anti-CD20 antibodies was known to be the same at the time the invention was made.

Further, Applicant reiterates arguments drawn to different modes of action and the requirement for FcR-expressing NK cells for the apoptotic mechanism of action of anti-CD20 antibodies and apparently argues that at the time the invention was made, the activity of FcR expressing NK cells in the CNS was uncertain. The argument has been considered but has not been found persuasive because no evidence has been presented demonstrating the uncertainty of activity of NK cells in the CNS at the time the invention was made.

In addition, it is noted that US Patent No. 5,776,456 specifically teaches the efficacy of treatment with radiolabeled antibodies specific for CD20. Although claims 56-60 and 62-68 do not specifically claim treatment with radiolabeled antibody, the claims as currently constituted recite the claimed method of treatment of claim 56 as comprising the step of administering a therapeutically effective amount of anti-CD20 antibody or fragment thereof, given the comprising language, the claims read on administering any anti-CD20 antibody or fragment thereof including radiolabeled antibodies. Thus, even if it were to be found that contrary to the teaching of Applicant's Declaration and the Shan et al reference, that anti-CD20 antibodies do not act through apoptotic mechanisms, it would be expected that the radiolabeled antibodies of US Patent No. 5,776,456 would effectively treat CNS lymphoma for the reasons previously set forth.

The arguments have been carefully considered but have not been found persuasive and the rejection is maintained.

6. Claims 56-60, 62-74 remain rejected under Obviousness Type Double Patenting for the reasons previously set forth in the paper mailed April 10, 2006, pages 5-6.

Applicant reiterates arguments as set forth above. The arguments have been considered but not found persuasive for the reasons set forth above.


7. It is noted that in the paper filed September 11, 2006 Applicant states that a "supplemental amendment and expert's declaration will follow shortly", however, neither a supplemental amendment nor an expert's declaration have been received.

7. No claims allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at 571-272-0787. The fax phone number for this Art Unit is (571) 273-8300.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.


Susan Ungar
Primary Patent Examiner
November 20, 2006